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Potency of Synthroid Tablets

TO THE EDITOR: The article "Maintenance Requirements of L-Thyroxine in the Treatment of Hypothyroidism" by W.A. Kehoe, B.J. Dong and F.S. Greenspan,[1] in the June 1984 issue, contains an addendum which has some incorrect statements that may be misleading to your readers.

The addendum states that Synthroid tablets were reformulated in 1983. In fact, the reformulation took place in 1982. Flint Laboratories' studies show that the bioavailability of the reformulated tablets averages 74%, compared to 70% for the old formulation. The figures of 78% and 100% given in the addendum are actually those reported not for bioavailability but for potency by Stoffer and Szpunar.[2] These potency estimates were, however, based on immunoassay, a technique that has not been validated for measurement of tablet potency. When official USP methodology is used, the potency of Synthroid tablets has not changed with the reformulation.

I hope this will clarify matters for your readers.

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Drs Kehoe, Dong and Greenspan Reply

TO THE EDITOR: We are grateful to Dr Horwitz for formally announcing that their product was reformulated in 1982. We are also pleased to know that it is not the bioavailability that has been changed, although L-thyroxine absorption is very variable.[1-3] However, our clinical experience in 1983-84 of increased biologic potency in patients previously maintained on a stable dose of L-thyroxine is similar to that observed by *Medical Letter* endocrinology consultants[4] and tends to agree with the findings reported by Sawin and co-workers[5] and Stoffer and associates.[6] Sawin and co-workers noted that the actual content of Synthroid tablets prior to reformulation contained 20% to 30% less than their stated content as measured by radioimmunoassay while Synthroid after reformulation contained 100% of the stated amount.[6] Interestingly, both studies were able to correlate the decreased tablet content with decreased response as measured by thyroid function tests.

We do not understand why there should be significant discrepancy in measuring tablet content between high-pressure liquid chromatography (HPLC) and radioimmunoassay but caution that patients previously maintained on a stable dose of L-thyroxine (Synthroid manufactured prior to 1982) may need readjustment of their dose downward to avoid clinical toxicity when receiving the newly reformulated L-thyroxine tablets.

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The Effect of Heparin Dilution on Arterial Blood Gas Analysis

TO THE EDITOR: Drs Dake, Peters and Teague[1] recently published an informative letter about artifacts in arterial blood gas measurements due to dilution with heparin solution. Their information agrees with data published by Dr James Hansen and me,[2] but there are points which I disagree with or wish to clarify.

Adding heparin solution to blood dilutes plasma carbonic acid (H_2CO_3) and, therefore, carbon dioxide; the measured carbon dioxide pressure (Pco_2) then will decrease in proportion to the amount of dilution, as the authors state. I disagree that "when excessive amounts of heparin are added . . . $Paco_2$ [arterial carbon dioxide pressure] is the measurement most profoundly affected," because concentrations of bicarbonate and base excess decrease proportionately with Pco_2. Equal dilution of Pco_2 and bicarbonate accounts for the fact that pH is unaffected, as the authors report. These dilutions change the "metabolic" and "respiratory" components of acid-base measurements proportionately, accounting for clinically unexplained stimultaneous mild primary respiratory alkalosis and primary metabolic acidosis. I agree that pH is also not affected measurably by adding acidic heparin, since the buffering capacity of heparin solution is much less than that of blood.

I disagree on two other points. I think it is incorrect to state that "the partial pressure of a gas in solution is proportional to the solubility coefficient of the gas and the partial pressure of the gas overlying the liquid." The partial pressure of a gas in solution is the same as the partial pressure of the gas overlying the liquid following equilibration. The solubility coefficient could affect partial pressure only indirectly if the gas dissolved significantly, decreasing the amount and partial pressure of the gas overlying the liquid. In the case of CO_2 this would be at most only a miniscule factor.

However, with the high "solubility coefficient" of oxygen in blood, dilution could have a significant effect on measured oxygen pressure (Po_2). We found this effect to be somewhat different from that reported by Dake and co-workers. Unpublished data from our laboratory suggest that the effect of